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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,376	07/20/2001	Chi-Huey Wong	TSRI 663.1	4021

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EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 06/04/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/762,376

Applicant(s)

WONG ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7 and 8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10. 6) ☐ Other: _____

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DETAILED ACTION

Claims 7 and 8 are currently pending in this application.

Election/Restrictions

Applicant's election without traverse of Group 2 claims 7-8 in Paper No. 14 is acknowledged.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Objections

Claim 8 is objected to because of the following informalities: The first letter of the name of the bacteria is recited as a small letter as opposed to the use of a capital letter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7-8 are drawn to a method of converting a substrate of the polysialyltransferase in to a product. However, applicants do not recite the specific substrate and the specific product that needs to be formed in the above reaction. Without any information regarding the acceptor and the donor for the transferase enzyme, the claim is unclear to the Examiner.

Claims 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7-8 recite the phrase "under conditions for promoting enzymic catalysis...". The metes and bounds or the scope of the above phrase in the context of the claim is unclear to the Examiner.

Claims 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7-8 recite the phrase "converting a substrate" and "a product". The metes and bounds or the scope of the above tow phrases in the context of the claim is unclear to the Examiner. It is not clear to the Examiner as to what type of substrates are encompassed by the claim. Similarly it is also not clear as to what type of products are encompassed by the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making polysialic acid homopolymers composed of unbranched sialyl- α 2,8/2,9 linkages by transferring monomeric sialic acid (N-acetylneuraminic acid) to the growing chain using an polysialyltransferase enzyme specifically isolated from *E.coli* K92, does not reasonably provide enablement for making any "product" by converting any "substrate" with any type of linkage associated with the product using any polysialyltransferase isolated from any source (claim 7) or does not reasonably provide enablement for a method of making any product using any substrate and using an enzyme isolated from *E.coli* K92 (claim 8). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 7-8 are so broad as to encompass the making of any "product" using any substrate and using either any polysialyltransferase from any source or a polysialyltransferase from *E.coli* K92. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of "products", "substrates" and enzymes

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from any or all sources broadly encompassed by the claims including variants, mutants and recombinants. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the making of a polysialic acid from sialic acid monomers which are linked by alternating α 2,8/2,9 linkage, using the polysialyltransferase isolated specifically from *E.coli* K92. It would require undue experimentation of the skilled artisan to make and use the claimed "products" using any "substrate" and any or all polysialyltransferase from any source. The specification is limited to teaching the use of the specific polysialyltransferase isolated from *E.coli* K92 for making polysialic acid but provides no guidance with regard to the making of any product using any substrate. In view of the great breadth of the claim, amount of experimentation required to perform the above method, the lack of guidance, working examples, and unpredictability of the art in predicting function of a polypeptide from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the method encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims,

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and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass the making of any product using any substrate using any of all polysialyltransferase from any source because the specification does not establish: (A) regions of the protein structure which may be modified without effecting its activity; (B) the general tolerance of polysialyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in a polysialyltransferase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including enzymes with an enormous number of amino acid modifications or from any source for making any "product". The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the use of the method is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

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Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 7-8 are directed to a method of making a product (polysialic acid) using a polypeptide with α 2,8/2,9 sialyltransferase activity. Claims 7-8 are rejected under this section of 35 USC 112 because the claims are directed to a method which uses a genus of polypeptides including modified polypeptide sequences --modified by at least one of deletion, addition, insertion and substitution of an amino acid residue-- that have not been disclosed in the specification. No description has been provided of the polypeptide sequences encompassed by the claim. No information, beyond the characterization of its function has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structure. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

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Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Vann WF (FEMS Microbiology Lett., 1995, Vol. 128(2):163-166) and Steenbergen et al. (J.Bacteriol., 1992; Vol. 174(4):1099-1108). This rejection is based on the public availability of a printed document.


Claims 7-8 of the instant application are drawn to a method of making polysialic acid product linked through α 2,8/2,9 linkage catalyzed by the α 2,8/2,9-polysialyltransferase isolated from *E.coli* K92. It is well recognized in the art that the above strain of *E.coli* produces a unique polysialyltransferase which links sialic acid monomers through an alternate α 2,8/2,9 linkage. The above two references disclose the purification and characterization of the polysialyltransferase from *E.coli* K92 and describes the method of making polysialic acid product using filter assays and/or gel filtration. Both the above references disclose the transfer of ¹⁴C-labeled sialic acid to endogenous or exogenous (colominic acid) acceptors forming the polysialic acid products. Therefore, Vann WF and /or Steenbergen et al. anticipate claims 7-8 of this application as written.

Conclusion

None of the claims are allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.


MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
June 4, 2003